

Coronavirus (COVID-19) and Pregnancy: What Maternal-Fetal Medicine Subspecialists Need to Know

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On March 11, 2020, the World Health Organization declared the COVID-19 outbreak [caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)] a pandemic. In light of this declaration, communication to obstetric care providers about this disease and how best to advise pregnant women is imperative. This document complements the recent <u>American College of</u> <u>Obstetricians and Gynecologists (ACOG) Practice Advisory</u> and rapidly evolving guidance from the Centers for Disease Control and Prevention (CDC) on this topic, with a specific focus on maternal, fetal, and neonatal implications.¹

How is COVID-19 spread?

COVID-19 likely emerged from an animal source but now is spreading from person to person.² Human coronaviruses can spread from an infected person to others through a variety of means, such as droplets from coughing and sneezing; close personal contact, including touching and shaking hands; and touching one's nose, mouth, or eyes before washing one's hands. It is currently unknown if the virus can be spread through semen, vaginal secretions, or sexual intercourse. Transmission from contact with an asymptomatic infected person has also been described and the extent of the spread is unknown.

Infection prevention measures are of critical importance for preventing the spread of infection. The CDC provides general recommendations for infection prevention in the management of COVID-19³ (<u>https://www.cdc.gov/coronavirus/2019-ncov/infection-control/control-</u> <u>recommendations.html</u>) as well as specific guidance for inpatient obstetric care⁴ (<u>https://www.cdc.gov/coronavirus/2019-ncov/hcp/inpatient-obstetric-healthcare-</u> <u>guidance.html</u>).

What is known about COVID-19 in pregnancy?

Currently, there is limited information from published scientific reports about the susceptibility of pregnant women to COVID-19 and severity of infection. Available data are still limited to small case series. In general, pregnant women experience immunologic and physiologic changes that make them more susceptible to viral respiratory infections. The initial characterization of pregnant women as a high-risk group was based largely on this fact, as well as on historical experience with other viruses. Pregnant women have been reported to be at greater risk for severe illness, morbidity, or mortality compared with the general population with related coronavirus infections [including severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV)] and other viral respiratory infections, such as influenza.^{5, 6} Early in the COVID-19 pandemic, two small case series from China described potentially lower risk in pregnant women, but these series included a total of only 18 patients and

must be interpreted with caution^{7, 8}. At present, there is no evidence that pregnancy increases a woman's risk of acquiring COVID-19 or developing severe symptoms from the disease.

Anecdotal experience in the United States indicates that pregnant women are as likely as the general public to develop symptoms if infected with coronavirus; symptoms are likely to be mild to moderate, as is true for nonpregnant individuals in this age range. Severe symptoms have also been reported in pregnant women, particularly those with comorbidities such as asthma or diabetes.⁹

Who should be tested for COVID-19?

Clinical judgment, local test availability, community spread, and other local policies should be used to decide which patients are tested for COVID-19.¹⁰ Signs and symptoms of COVID-19 range from mild to severe and include fever, myalgias, cough, and difficulty breathing as well as gastrointestinal symptoms and anosmia in some patients. According to the CDC, epidemiologic factors, such as the prevalence of COVID-19 in the local community, may also be used to guide testing.

As of April 4, 2020, the CDC guidance recommends that pregnant women admitted with suspected COVID-19 or who develop symptoms concerning for COVID-19 during admission should be prioritized for testing. Clinicians are also encouraged to test these women for other causes of respiratory illness, as appropriate. COVID-19 testing recommendations are likely to change frequently, and maternal-fetal medicine (MFM) subspecialists are encouraged to test the CDC website for evolving guidance.¹⁰ For more information, please refer to the CDC guidance Evaluating and Testing Persons for Coronavirus Disease 2019 (COVID-19).

Current testing for COVID-19 is by polymerase chain reaction (PCR), and availability varies by location. Health care providers or facilities should notify their local or state health department when evaluating a person under investigation (PUI) for COVID-19. As testing availability increases, this guidance may be subject to change.

Is there evidence of vertical transmission of COVID-19?

In one study evaluating the question of vertical transmission, Chen et al found no evidence of COVID-19 in the amniotic fluid or cord blood of 6 infants of infected women.⁸ Although this report includes only a small number of cases, the lack of vertical transmission is consistent with observations from other common respiratory viral illnesses during pregnancy, such as influenza. Recent reports describe a few neonates with either an elevated IgM or positive PCR result for COVID-19. However, it is not clear that these cases actually represent vertical transmission, and further study is needed.^{11, 12}

Does COVID-19 cause miscarriage or congenital anomalies?

At this time, very limited data regarding risks associated with infection in the first and second trimesters exist. There are mixed data regarding the risk of congenital malformations in the setting of maternal fever in general. Currently, there are inadequate data about COVID-19 and the risk of miscarriage or congenital anomalies. Data from the SARS-CoV epidemic are reassuring, suggesting no increased risk of fetal loss or congenital anomalies associated with infection early in pregnancy.¹³

Are women infected with COVID-19 at increased risk for preterm birth?

Preterm delivery has been reported among women positive for COVID-19 during pregnancy. However, it appears that some of these cases may be iatrogenic and not due to spontaneous Given the limited data available regarding COVID-19 during pregnancy, adverse obstetrical and perinatal outcomes reported with other respiratory viral infections have been extrapolated to COVID-19. Other respiratory viral infections during pregnancy, such as influenza, have been associated with adverse neonatal outcomes, including low birth weight and preterm birth, generally thought to be due to severe maternal illness. Infants have been born preterm, small for gestational age, or both to women with other coronavirus infections, including SARS-CoV and MERS- CoV, during pregnancy.^{5, 6} However, it is not clear that the implications and outcomes associated with COVID-19 are the same as with these other infections. Further data are urgently needed.

Do women with COVID-19 need additional antenatal surveillance?

During acute illness, fetal management should be similar to that provided to any critically ill pregnant woman. Continuous fetal monitoring in the setting of severe illness should be considered only after fetal viability, when delivery would not compromise maternal health or as another noninvasive measure of maternal status.

Very little is known about the natural history of pregnancy after a patient recovers from COVID-19. In the setting of a mild infection, management similar to that for a patient recovering from influenza is reasonable. It should be emphasized that patients can decompensate after several days of apparently mild illness, and women should be instructed to call or be seen for care if symptoms, particularly shortness of breath, worsen. Given how little is known about this infection, a detailed midtrimester anatomy ultrasound examination may be considered following first-trimester maternal infection. For those experiencing illness later in pregnancy, it is reasonable to consider ultrasonographic assessment of fetal growth in the third trimester. Please see <u>The Society for Maternal-Fetal Medicine COVID-19 Ultrasound Practice Suggestions</u> for further information. Signs and symptoms of preterm labor should also be reviewed.

Are there delivery considerations?

In general, maternal COVID-19 infection itself is not an indication for delivery.⁸ Timing of delivery, in most cases, should not be dictated by maternal COVID-19 infection. For women infected early in pregnancy who recover, no alteration to the usual timing of delivery is necessary. For women infected in the third trimester who recover, it is reasonable to attempt to postpone delivery (if no other medical indications arise) either until a negative testing result is obtained or quarantine status is lifted to avoid potentially separating mother and infant and to decrease potential health care worker exposures. For women who are critically ill, preterm delivery may be considered if it is thought that it could potentially improve maternal status.

For additional intrapartum recommendations, please refer to <u>Society for Maternal-Fetal Medicine</u> and Society for Obstetric and Anesthesia and Perinatology Labor and Delivery COVID-19 <u>Considerations.</u>

What protective measures can be taken for the neonate?

At this time, the CDC recommends that infants born to mothers with known COVID-19 at the time of delivery should be considered to have suspected COVID-19 and should be tested and isolated from other healthy infants. The determination of whether to keep a mother with known or suspected COVID-19 and her infant together or separated after birth should be made on a case-by-case basis, using shared decision-making between the mother and the

clinical team⁴ (<u>https://www.cdc.gov/coronavirus/2019-ncov/hcp/inpatient-obstetric-healthcare-guidance.html</u>). Providers are encouraged to check the CDC site frequently regarding this topic, as new guidance is added daily.

What are postpartum considerations for PUI/COVID positive woman?

As with other infected individuals, management of postpartum women depends on the severity of their symptoms. Women with mild symptoms can recover at home, while those with more severe symptoms, including shortness of breath, may require hospitalization.¹⁵ Please refer to the <u>CDC</u> and <u>American Academy of Pediatrics</u> for guidance regarding care of the newborn after discharge. As with prenatal visits, monitoring of the postpartum woman can include the use of telehealth. For any individual who develops symptoms of COVID-19, self-quarantine is important to avoid transmission to others, including family members. It should again be emphasized that patients can decompensate after several days of apparently mild illness, and women should be instructed to call or be seen for care if symptoms worsen.

Can an infected woman breastfeed?

Chen et al found no evidence of COVID-19 in the breast milk of 9 infected women.⁸ Breastfeeding is encouraged and is a potentially important source of antibody protection for the infant. The CDC recommends that during temporary separation, women who intend to breastfeed should be encouraged to express their breast milk to establish and maintain milk supply. If possible, a dedicated breast pump should be provided. Before expressing breast milk, women should practice appropriate hand hygiene. After pumping, all parts of the pump that come into contact with breast milk should be thoroughly washed, and the entire pump should be appropriately disinfected per the manufacturer's instructions. Expressed breast milk should be fed to the newborn by a healthy caregiver. For women and infants who are not separated, the CDC recommends that if a woman and newborn do room-in and the woman wishes to feed at the breast, she should put on a facemask and practice hand hygiene before each feeding⁴ (https://www.cdc.gov/coronavirus/2019-ncov/hcp/inpatient-obstetric-healthcareguidance.html).

Are there treatments for COVID-19?

Currently, no medications are approved for the treatment of COVID-19 by the US Food and Drug Administration. A number of medications approved for other indications as well as several investigational drugs are being studied in clinical trials. Drugs that have been considered or are under investigation for the treatment of COVID-19 include hydroxychloroquine (with or without azithromycin), remdesivir, tocilizumab, sarilumab, and convalescent plasma.

Hydroxychloroquine and chloroquine, which are used in the treatment of malaria and some inflammatory conditions such as systemic lupus erythematosus, also have in vitro activity against SARS-CoV-2 and other coronaviruses. Chloroquine was shown in one small study to decrease detection of SARS-CoV-2 RNA in upper respiratory tract specimens when administered with or without azithromycin. However, the study was very small, clinical benefit was not assessed, and subsequent studies are conflicting. Hydroxychloroquine and chloroquine are associated with QT prolongation and caution is advised if consideration is given to using these drugs in patients with chronic medical conditions.^{16,17}

Remdesivir is an antiviral drug that has in vitro activity against SARS-CoV-2, as well as in vivo activity against other related betacoronaviruses. A number of clinical trials of this agent are

underway, and it is also available on a compassionate-use basis, including in pregnant women. An expanded access program is also in development.

Tocilizumab and sarilumab are human monoclonal antibodies against the IL-6 receptor, intended to target the cytokine release syndrome associated with COVID-19. Tocilizumab is already approved by the FDA for the treatment of cytokine release syndrome (CRS) that is severe or life-threatening. A number of clinical trials of this agent are currently underway.

Convalescent plasma is collected from individuals who have recovered from COVID-19, given the likely presence of antibodies against SARS-CoV2. Convalescent plasma has been used in prior viral respiratory illness epidemics, including H1N1 influenza, SARS-CoV, and MERS-CoV. Although promising, convalescent plasma has not yet been shown to be effective in COVID-19.¹⁸

At present, no vaccine exists for COVID-19, although efforts are underway to develop a vaccine as quickly as possible.

Should obstetric care appointments be altered?

Alternate prenatal care schedules have been proposed as a strategy to control the spread of COVID-19. Community mitigation efforts are important, although the implementation of such strategies depends on local practice and population factors and resources. Where available, telehealth (including telephonic and other remote services) can be used to allow access to care for these patients while implementing community mitigation efforts. Obstetrician-gynecologists and other prenatal care practitioners should ensure that patients with certain high-risk conditions continue to be provided necessary prenatal care and antenatal surveillance when indicated.

What is the guidance for pregnant healthcare personnel?

Pregnant health care personnel (HCP) should follow the CDC risk assessment and infection control guidelines for HCP with potential exposure to patients with suspected or confirmed COVID-19. While pregnant HCP may continue to work, facilities may consider limiting their exposure to patients with confirmed or suspected COVID-19, especially during higher-risk procedures (eg, aerosol-generating procedures). However, in settings with a higher burden of disease or limited staffing, this may not be feasible. The above recommendations should also be applied to other HCP considered to be at higher risk for severe complications of infection, such as older adults; people with chronic medical conditions (heart disease, diabetes, and lung disease); or those who are immunocompromised.

<u>Summary</u>

It is important for MFM subspecialists to learn about COVID-19 to optimize patient care and to protect themselves. This is a rapidly changing landscape, and new information will continue to be updated frequently. As data on pregnancy accumulate, SMFM will continue to provide guidance to our members.

For questions related to labor and delivery considerations and ultrasound practice suggestions during the COVID-19 pandemic, please refer to SMFM's other resources:

Society for Maternal-Fetal Medicine and Society for Obstetric and Anesthesia and Perinatology Labor and Delivery COVID-19 Considerations

The Society for Maternal-Fetal Medicine COVID-19 Ultrasound Practice Suggestions

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